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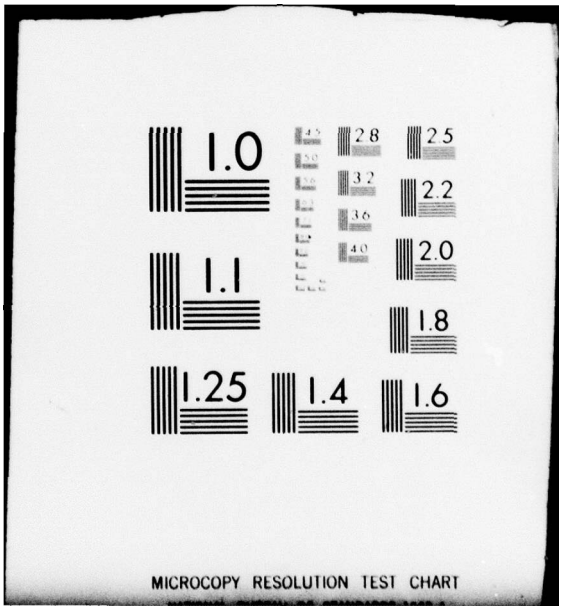
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Population Genetics of Hemoglobin E, Thalassemia and Related Genetic Polymorphisms in Thailand

Final Report

(1965 - 1970)

March 1978

by

Donald L. Rucknagel, M. D.

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The Thai population data have been analyzed using the following general approach. The phenotype frequency was determined for all of the genes after separating the Thais from hill tribesmen. From the total Thai sample we then removed first the children and then related adults. The frequency of genetic traits in the total or corrected samples did not differ significantly. These manipulations were necessary to deal with the randomness of the samples, because even truly random samples of small endogamous populations will contain relatives. Since we did not know precisely the mating structure of our populations we had no other more direct approach to the question of whether we had ascertained an inordinate number of relatives. We then calculated gene frequencies for each genetic system in each village and in each province and compared them statistically and for adherence to the Hardy-Weinberg equilibrium.

The anthropometrics and other quantitative variables such as uric acid and serum iron levels were analyzed by regressing onto age and then comparing between groups by covariance analysis. Group comparisons included comparisons between provinces in Thailand, between sexes, and for attributes such as serum iron and hemoglobin levels between the hemoglobin E, thalassemia, and normal phenotypes.

In view of the complexity of the study a table is appended to demonstrate some of the findings. First, there is a great deal of heterogeneity in gene frequency within provinces in Thailand (not shown in the table) which cannot be attributed to small sample size. Despite this variation, gene frequencies appear to vary systematically in the country as judged from the ten provinces which we have studied. In Northeastern Thailand, in addition to the high frequency of Hb E, the Thai electrophoretic variant on ceruloplasmin, transferrin D, blood groups Ms, and secretor are more frequent than in other areas; Lewis (a+b-), and 6-phosphogluconate dehydrogenase type B are somewhat less frequent. Frequencies in Surin are strikingly out of line with those elsewhere in Northeastern Thailand, suggesting that Cambodians are somewhat different. For instance, the frequencies of ceruloplasmin Thai, secretor, Lewis (a-b-), and blood group B are greater; blood groups O and Ns are less frequent than elsewhere in this region.

In Northern Thailand the beta-thalassemia gene is most frequent. This does not appear to be derived from the hill tribesmen inasmuch as it was nearly absent from our small series of tribesmen. This region is characterized by elevated levels of glucose-6-phosphate dehydrogenase deficiency, Diego blood group, and Ms, the lower frequencies of 6-phosphogluconate type B, secretor, blood group B, and MS.

Southern Thailand is characterized by an elevated frequency of MS, and lower frequencies of hemoglobin E, G-6-PD deficiency, Ms, and Lewis (a-b-) than in most other areas.

The analysis of anthropometric measurements shows a large number of non-systematic differences between provinces.

Some systematic differences are apparent, however. For instance, individuals in Northern Thailand appear significantly smaller than those examined elsewhere in the country. Interpretation of these differences will be difficult, until statistical inter-racial distance measurements are completed; these are in progress.

The differences in gene frequencies outlined suggest that genetic drift and founder effect play a large role in so-called microdifferentiation within provinces. Whereas the differences in gene frequencies in the various provinces do not correlate perfectly, the fact that so many gene frequencies vary so much from one region to another suggests that this variation is more likely to be due to gene flow or migration rather than differential selective values throughout the country. If, for instance, the high frequency of thalassemia were the only characteristic of the Northern Thai, malaria selection pressure would be a reasonable explanation. If a rational relationship were apparent for several other genetic characteristics in this area, one might still invoke selection. For instance, malaria might select for genetic mutants of the hemoglobin, glucose-6-phosphate dehydrogenase, and haptoglobin loci since all three of these proteins are involved with the integrity of the red blood cell. We have no rational basis for invoking entities such as the blood groups, for instance, also in a selection model. Migration seems a more likely common denominator.

The gene frequency data have been collated, and the terminal report is being prepared on the descriptive aspects of the study. The fertility data have been analyzed in a preliminary fashion but set aside for the moment because they present special problems in analysis for which we have not as yet worked out the methodology.

Gene Frequencies

	HbE	β-Thal	6-PGD	Tf-D	Gc-1	Hp-1	Cp-Th	B	O	Ms	MS	Di[a]	Sec.	Le (a+b-)
Central														
Saraburi	.11	.03	.07	.01	.54	.22	.09	.19	.62	.66	.04	.0	.39	.54
Khanchanaburi	.06	.01	.07	.06	.64	.29	.07	.21	.60	.66	.07	.01	.44	.55
Northeast														
Pak Chong	.20	.004	.06	.06	.75	.28	.21	.21	.61	.69	.06	.01	.47	.49
Chum Pae	.23	.005	.05	.10	.76	.24	.18	.22	.64	.71	.04	.003	.49	.60
Udorn	.15	.010	.03	.07	.73	.24	.15	.22	.63	.74	.02	.02	.50	.52
Surin	.26	.010	.04	.07	.73	.23	.21	.35	.49	.72	.09	.01	.58	.52
North														
Chiengmai	.03	.04	.02	.02	.74	.29	.27	.17	.70	.71	.03	.04	.44	.66
Tak	.06	.01	.04	.04	.71	.20	.17	.24	.63	.60	.11	.02	.48	.63
Lom Sak	.22	.01	.04	.06	.71	.25	.18	.26	.63	.67	.06	.01	.53	.49
South														
Nakorn Srithamarat	.06	.01	.04	.04	.74	.20	.14	.21	.64	.58	.10	.002	.45	.59

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Literature Cited.

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Shokeir, M. A., Rucknagel, D. L., Na-Nakorn, S., Wasi, P., and Shreffler, D. C.: Genetic polymorphism of human serum ceruloplasmin in Thailand. Amer. J. Hum. Genet., in press.

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